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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Levenberg <i>et al.</i>	Examiner:	Sgagias, M.K.
Serial Number:	10/731,672	Art Unit:	1632
Filed:	December 9, 2003		
For:	ENGINEERING THREE-DIMENSIONAL TISSUE STRUCTURES USING DIFFERENTIATING EMBRYONIC STEM CELLS		

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Declaration under 37 C.F.R. § 1.131

I, Shulamit Levenberg, Ph.D., declare as follows:

1. I am currently an Associate Professor in Biomedical Engineering Department at Technion, Israel Institute of Technology, Israel. I received my Ph.D. from Weizmann Institute of Science, Rehovot, Israel in Molecular Cell Biology in 1999, and worked in Prof. Robert Langer Lab at Massachusetts Institute of Technology, U.S.A., from 1999 to 2004.
2. I am an inventor of the subject matter disclosed and claimed in the present application, U.S.S.N. 10/731,672, filed December 9, 2003, and entitled "ENGINEERING THREE-DIMENSIONAL TISSUE STRUCTURES USING DIFFERENTIATING EMBRYONIC STEM CELLS" (the '672 application). This application claims priority to U.S. Provisional Patent Application Serial No. 60/432,228, filed on December 10, 2002 (the '228 application), and U.S. Provisional Patent Application Serial No. 60/443,926, filed on January 31, 2003 (the '926 application).
3. This declaration is presented for the purpose of removing from consideration by the Examiner the reference by Griffith, *et al.* (Science, 295: 1009-1014, 2002) (hereafter "Griffith"). This article bears a publication date of February 8, 2002. Therefore, Griffith became available to

the public less than one year prior to the filings of the '228 application and the '926 application, to which the present application claims priority.

4. The present Declaration is presented in accordance with *In re Stempel*, 113 U.S.P.Q. 77 (CCPA 1957) and establishes conception and reduction to practice of the invention in this country before February 8, 2002, the effective date of the cited Griffith.

5. On a date before February 8, 2002, I, together with co-inventors Ngan F. Huang, Erin B. Lavik, Joseph Itskovitz-eldor, and Robert Langer conceived and reduced to practice tissue engineering constructs comprising embryonic stem cells, a three-dimensional cell support polymer matrix, and at least one growth factor selected to promote differentiation of the stem cells, and methods thereof.

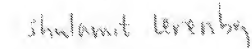
6. **Exhibit A** is a copy of two pages from my laboratory notebook, with dates blacked out. Exhibit A provides evidence of conception and actual reduction to practice of tissue engineering constructs comprising embryonic stem cells, a porous three-dimensional cell support polymer matrix, and at least one growth factor selected to promote differentiation of the stem cells, and methods thereof prior to February 8, 2002.

7. **Exhibit A** includes a description of experiments in which exemplary growth factors were used to differentiate stem cells on polymer scaffolds into tissue-like structures. The first page shows the details of preparation of polymer scaffolds and stem cells from embryoid bodies (EBs) with different growth factors. The second page shows results of seeding stem cells onto the polymer scaffolds with growth factors. For example, retinoic acid (RA), a growth factor, was added to form neural tissues. The dates on which the experiments were performed are found on the notebook, and are prior to February 8, 2002.

8. The laboratory notebook pages were prepared in the United States of America.

9. I declare that all statements made herein of my own knowledge are true, and that those statements made on information and belief are believed to be true; and further that these

statements were made with the knowledge that willful, false statements and the like are made punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful, false statements may jeopardize the validity of the '542 application or any patents that may issue thereon.

A handwritten signature in dark ink, appearing to read "Shulamit Levenberg". The signature is written in a cursive, somewhat stylized script.

Shulamit Levenberg, Ph.D.

6 July 2010
Date